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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO: | CONFIRMATION NO. |
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Norman H. Stepno, Esquire
BURNS, DOANE, SWECKER & MATHIS, L.L.P.
P.O. Box 1404
Alexandria, VA 22313-1404

| EXAMINER | |
|---|---|
| FISHER, LATONIA M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/020,184 | RAO ET AL. | |
| | Examiner | Art Unit | |
| | La Tonia M. Fisher | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-67 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-67 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

Claims 1-67 are pending.

### *Claim Objections*

Claim18 is objected to because of the following informalities: The claim appears to have a typographical error. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, and 4-13, 37, 40, 43 and 64-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the wording "which is further provided and oily matrix..."is awkward and ambiguous. Thus, claim 2 and all claims depending on claim 2, here claims 5-13, are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The wording "depending on assay, potency, moisture content and overage" in claims 4 and 37 is superfluous and should be deleted. It fails to patentably impact the range in amount of SAMe set forth in the claim.

Claims 7, 10, 40 and 43 recite a broad recitation with narrow recitation. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat.

App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 7 recites the broad recitation 15 to 20%, and the claim also recites preferably 16% which is the narrower statement of the range/limitation. Claim 10 recites the broad recitation 50 to 55% and the claim also recites preferably 53%, which is the narrower statement of the range/limitation. Claim 40 recites the broad recitation 15 to 20%, and the claim also recites preferably 16%, which is the narrower statement of the range/limitation. Claim 43 recites the broad recitation 50 to 55% and the claim also recites preferably 53%, which is the narrower statement of the range/limitation.

In claims 64 and 65, the terms "device" and "opacifying agent" lack antecedent basis.

Please note that all claims which depend from an indefinite claim and fail to remedy said claim's deficiencies under 35 USC 112, Second Paragraph as set forth herein, are also rejected for the reasons of record.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adusumilli et al. (USPN 5,595,758) in view of Zappia et al. (USPN 4,764,603) and Fiecchi (USPN 3,954,726).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-34 are drawn to a soft gelatin capsule comprising S-adenosylmethionine (SAMe) salt. Dependent limitations claimed include the identity of the core of the gelatin capsule, specific SAMe salts, the amount of SAMe, lipophilic material specifics, the amount of lipophilic materials, additional composition components such as antioxidants, preservatives, softening agents, plasticizers, opacifying agents, preservatives, and coloring agents, additional

composition component specifics, the amounts of these components, the type of enteric coating on the capsule and the amount, pH and thickness of the enteric coating.

Andusumilli et al. teaches single piece soft gelatin capsules comprising softening agents, plasticizers, opacifying agents, stabilizers, preservatives, antioxidants and coloring agents including vegetable oils, glycerin, polyhydric alcohols and their esters, polycarbonates, waxes, vitamins, minerals, amino acid supplements and light absorbing agents, and methods for preparing said capsules. See USPN '758, col. 2, lines 59-60 and col. 3, lines 5-68. Furthermore, Andusumilli et al. teaches that the active agent particles of the prior art soft gelatin capsules be present in an amount which fills up to 90% of the internal volume of the capsule. See USPN '758, col. 7, lines 10-14. In column 4 at lines 46-49, Andusumilli et al. teaches that the active agent can be comprised of pure agent, or as will often be the case, coated with a protective layer which may or may not affect how fast the particle dissolves and releases the active ingredient. Andusumilli et al. also discloses the release characteristics of the dose form of lipophilic drugs can be immediate release of entire dose or a combination of immediate release of the loading dose and sustained release of the maintenance dose to satisfy the required therapeutic response. See USPN '758, col. 5, lines 61-68 to col.6, lines 1-2.

Andusumilli et al. does not teach a soft gelatin capsule comprising S-adenosylmethionine (SAMe) salt.

Capsules containing SAMe are well known in the art. Zappia et al. teaches capsules containing SAMe salts. See USPN '603, col. 13, lines 24-27 and col. 14, claim 12. Fiecchi teaches capsules containing SAMe salts prepared with sulphuric acid and p-toluenesulphonic acid. See USPN '726, col. 15, lines 31-33 and col. 16, claims 1-13.

Thus, it would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a soft gelatin capsule having enteric coating and comprising S-adnosylmethionine as applicants have done with the references before them. Applicants would have been motivated to prepare soft gelatin capsules comprising SAMe salts since Adusumilli et al. teaches that bio-availability of extremely water insoluble highly lipophilic drug substances, for example, SAMe, can be enhanced using the soft-shelled gelatin dosage form. See USPN '758, col. 6, lines 43-44.

Claims 35-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adusumilli et al. (USPN 5,595,758) in view of Matthews et al. (USPN4, 816,259), Zappia et al. (USPN 4,764,603) and Fiecchi (USPN 3,954,726).

Claims 35-67 are drawn to methods for preparing a soft gelatin capsule comprising SAMe, comprising coating SAMe salt with a lipophilic material to obtain granules, coating the granules with an oily matrix, antioxidants and preservatives to form a liquid suspension, disposing the liquid suspension within a soft gelatin film, and coating the soft gelatin capsule with an enteric coating. Dependent limitations claimed include the identity of the core of the gelatin capsule, specific SAMe salts, the amount of SAMe, lipophilic material specifics, the amount of lipophilic materials, additional composition components such as antioxidants, preservatives, softening agents, plasticizers, opacifying agents, preservatives, and coloring agents, additional composition component specifics, the amounts of these components, the type of enteric coating on the capsule and the amount, pH and thickness of the enteric coating.

The examiner refers to the teachings of Andusumilli et al. cited above.

Matthews et al. teaches a process for coating a soft gelatin capsule shell comprising applying to the outer surface of said shell at least one continuous layer of a subcoating composition consisting essentially of hydroxypropyl methyl cellulose and polyethylene glycol and comprising titanium dioxide. See USPN '259, col. 4, lines 1-68 and col. 5, lines 1-10. Matthews et al. also discloses in column 1, lines 48-50 that enteric coatings are useful for producing a delayed action of a drug. Matthews et al. discloses that the capsules are prepared by admixing gelatin, glycerin and water into a wet mass which is thereafter manufactured into finished capsules and during the production of the wet gelatin mass for the preparation of the capsules, conventional additives, including plasticizers, coloring agents, opacifiers, fillers and preservatives such as parabens, may be optionally added. See USPN '259, col. 2 lines 13-25. Matthews et al. further discloses that the gelatin mass is prepared in a manner that produces a smooth completely dispersed gelatin suspension. See USPN '259, col. 2, lines 34-55. The suspension is then disposed within a soft gelatin film and the soft gelatin capsule is coated with enteric coating. USPN '259, col. 2, lines 56-66.

Neither Andusumilli et al. nor Matthews et al. teach a method of preparing a soft gelatin capsule comprising S-adenosylmethionine (SAMe) salt.

As mentioned earlier, capsules containing SAMe are well known in the art. Zappia et al. teaches capsules containing SAMe salts. See USPN '603, col. 13, lines 24-27 and col. 14, claim 12. Fiecchi teaches capsules containing SAMe salts prepared with sulphuric acid and p-toluenesulphonic acid. See USPN '726, col. 15, lines 31-33 and col. 16, claims 1-13.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to coat SAMe salt with a lipophilic material, form a liquid

suspension with art known agents, dispose the SAMe liquid suspension within a soft gelatin film and coat the soft gelatin capsule with enteric coating as applicants have done with the references before them.

***Conclusion***

Claims 1-67 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to La Tonia M. Fisher whose telephone number is (703) 306-5819. The examiner can normally be reached on Monday - Friday from 9:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (703) 308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600